

DESCRIPTION

A METHOD FOR TESTING PERITONEUM FUNCTION AND A PERITONEAL DIALYSIS PLANNING APPARATUS

Background of the Invention

1. Field of Invention

The present invention relates to a method for testing peritoneal function and a peritoneal dialysis planning apparatus using a computer.

2. Description of the Related Art

It is believed that there are presently about 200,000 patients with chronic renal failure in Japan. Of them, 92% to 93% receive hemodialysis as a maintenance treatment while the remaining 7% to 8% receive peritoneal dialysis.

"Dialysis" here means a process of removal of certain molecules from body fluid due to a concentration gradient by filtering it across a membrane, making use of different molecular weights. Thus, this process assists impaired renal function of the patients by dissolving various substances, which are accumulated in the body through metabolic activities—solutes (such as urea (U) as a uremic toxin and creatinine (Cr)), electrolytes (Ca^{2+} , Cl^- , Na^+ , and K^+), excess water and the like, out of the body fluid into a dialysis solution, and by then discharging the dialysis solution from the body as drained fluid. Two distinguished methods used for dialysis are hemodialysis (HD) and peritoneal dialysis (PD). Hemodialysis is a mechanical blood purification procedure to pass blood through the extracorporeal circulation, while peritoneal dialysis is a blood purification procedure achieved by infusing a dialysis solution into the peritoneal cavity and filtering blood through the peritoneum. Conventionally, either of the dialysis procedures can be applied to the patients. In the case when deficient renal function cannot be fully compensated, it is considered as desirable to perform extracorporeal dialysis treatment using hemodialysis.

With peritoneal dialysis, the patients perform dialysis treatment mainly at home. The home dialysis involves the repetition of the following steps several times a day: introduction of a dialysis solution into the peritoneal cavity performed by patients themselves using a catheter; retention of the introduced dialysis solution for several hours; and then drainage of the dialysis solution. The patient records the amount of excess water drained from the body (referred to as the "volume of water removal") every time a dialysis solution is drained, and submits the records to doctors in a subsequent medical examination to obtain a prescription. Such a peritoneal dialysis procedure is called CAPD (Continuous Ambulatory Peritoneal Dialysis). Doctors take particular note of the volume of water removal of the patients, and choose appropriate prescriptions for the patients based on the volume of the drained water.

A peritoneal dialysis system, in which a condition of patient's peritoneal function is simulated by a computer, has been developed in recent years (see Japanese Laid-Open Patent Application Publication No. 2000-140100). This peritoneal dialysis system enables testing aspects of peritoneal function, such as the rates of solute removal and transperitoneal water removal, by computing Pyle-Popovich's mathematical model, known as a macroscopic model of peritoneal dialysis, from patient's data—the concentration of each solute, the volume of water removal and so on included—obtained by using PET (Peritoneal Equilibration Test, 1987). In general, a commercially available personal computer is typically employed in an apparatus operating such a system.

The above-mentioned peritoneal dialysis system is, however, generally capable of only making a diagnosis either qualitatively or quantitatively, although it can assess peritoneal function of a patient at the time when data is collected, based on the concentration of each solute and the volume of water removal. Accordingly, it is very difficult to study future changes in patient's peritoneal function (so-called "a mechanism of deterioration in peritoneal permeability) by using such a system.

For example, as to data obtained from a patient, in the case when an apparent

volume of water removal indicated by a numerical value of the data is low, the following can be considered as possible causes. However, it is impossible to determine which of the following is/are the actual cause.

A: water is not drained out since the catheter tip inserted into the peritoneum is physically blocked or malpositioned (external factor);

B: the lymphatic system of the peritoneum has an elevated level of reabsorption capability; and

C: actual peritoneal function (the rate of transperitoneal water removal) has been reduced.

Of them, when *A* is the real cause, the blockage in the catheter is removed or the position is corrected, while anti-inflammatory agents are administered into the lymphatic system when *B* is the cause. If the cause is *C*, dialysis modality is switched from peritoneal dialysis to hemodialysis. Thus, the ways of handling the situation are much different depending on the real cause. In addition, when both *B* and *C* are the cause, the patient may possibly have complications with peritonitis or encapsulated peritoneal sclerosis, and therefore much consideration has to be given to how to treat the patient. Thus, conventional methods of testing peritoneal function do not fully allow critical judgments to be made to determine appropriate treatments for patients, and therefore, there is still room for improvement.

The present invention has been made in view of the above problems, and aims at offering a method for testing peritoneal function and a peritoneal dialysis planning apparatus which allow (i) an accurate analysis of a peritoneal function (a mechanism of deterioration in peritoneal permeability) of patients with peritoneal dialysis by using various types of data obtained through conventional methods and (ii) the application of the results of the analysis to future diagnostic prescriptions.

Brief Summary of the Invention

In order to solve the above problems, the present invention uses a ratio

$MTAC_{un}/MTAC_c$ calculated using $MTAC_{un}$ and $MTAC_c$ as an index for a peritoneal function test, where $MTAC_{un}$ is an overall mass transfer—area coefficient for urea nitrogen and $MTAC_c$ is an overall mass transfer—area coefficient for creatinine.

" $MTAC_{un}/c$ " denoted hereinafter means " $MTAC_{un}/MTAC_c$ ". For convenience of explanation, these notations are separately used depending on the situations.

In addition, the peritoneal function testing method of the present invention may further calculate a permeability coefficient for cell pores (L_{PS_C}) and an overall permeability coefficient (L_{PS}) from a Three-Pore Theory model while obtaining a ratio L_{PS_C}/L_{PS} calculated using the L_{PS_C} and the L_{PS} , and may use the L_{PS_C}/L_{PS} ratio and a volume of water removal as indexes for the peritoneal function test.

As a result of keen investigation using extensive data collected from actual patients with peritoneal dialysis, the inventors of the present invention found that, when the value of $MTAC_{un}/c$ is closer to 1 (i.e. the values of $MTAC_{un}$ and $MTAC_c$ are closer to each other), the permeability of the patient's peritoneal function has been more deteriorated and the volume of water removal is less. That is, while conventional testing is able to analyze only the amount of solute removal and the volume of water removal, the use of $MTAC_{un}/c$ of the present invention as described above enables examination of the future peritoneal function of a patient (a mechanism of deterioration in peritoneal function). The relation between $MTAC_{un}/c$ and the future peritoneal function of a patient can be proven by empirical data obtained from patients actually having complications with peritonitis and patients likely to have the complications in the future.

Additionally, since $MTAC_{un}/c$ is a dimensionless ratio, this parameter offers an advantage of being used in a mathematical model other than the Pyle-Popovich model, and furthermore allows a straightforward comparison between patients without requiring adjustment for variations in their physical attributes. Note that L_{PS_C}/L_{PS} to be hereinafter described is also a dimensionless parameter, and offers an expanded versatility.

In the peritoneal function testing method of the present invention, the $MTAC_{un}/MTAC_c$ ratio and a volume of water removal may be used as indexes for the peritoneal function test.

Thus, checking values of $MTAC_{un}/c$ and the volume of water removal virtually simultaneously enables a more detailed peritoneal function test to be made. To be more specific, for example, when the volume of water is low even if $MTAC_{un}/c$ is favorable, a reduction in peritoneal function other than the solute transfer (i.e. mainly, the rate of transperitoneal water removal) can be determined. This leads to an examination of the adequacy of switching to an efficient dialysis procedure in which unnecessary use of antiphlogistic drugs for peritonitis is avoided (i.e. a switch to hemodialysis from peritoneal dialysis). When neither $MTAC_{un}/c$ nor the volume of water removal is favorable, it is determined that peritoneal function has been severely damaged causing malignant failure, which allows a prompt transition of the dialysis procedure and quick countermeasures along with prescription of various antiphlogistic drugs. In the case when the volume of water removal is favorable while $MTAC_{un}/c$ is low, it is determined that peritoneal function is in a benign failure mode (that is, although the aquaporins are sufficiently active, the small and large pores with reversibility are exhausted and temporarily deactivated), which raises consideration of the necessity of rest.

In addition, the peritoneal function testing method of the present invention may further calculate a permeability coefficient for cell pores ($L_P S_C$) and an overall permeability coefficient ($L_P S$) from the Three-Pore Theory model while obtaining a ratio $L_P S_C/L_P S$ calculated using the $L_P S_C$ and the $L_P S$, and may use the $L_P S_C/L_P S$ ratio and a volume of water removal as indexes for the peritoneal function test.

Herewith, a further detailed peritoneal function test can be achieved. To be more specific, a ratio ($L_P S_C/L_P S$) of water permeability coefficient of aquaporins to the overall water permeability coefficient is obtained from the Three-Pore Theory model. $L_P S_C/L_P S$ is a ratio representing the activity power of the aquaporins, which is believed

to account for approximately 40% of the rate of transperitoneal water removal in pores in the capillary vessels of the peritoneum. The ratio taking a larger value means that the rate of the transperitoneal water removal is higher. A detailed diagnosis of peritoneal function is made possible by presenting a correlation of L_{PS_C}/L_{PS} with $MTAC_{un/c}$ or with the volume of water removal.

Furthermore, the present invention being a peritoneal function testing method using the Three-Pore Theory model may calculate a permeability coefficient for cell pores (L_{PS_C}) and an overall permeability coefficient (L_{PS}) while obtaining a ratio L_{PS_C}/L_{PS} calculated using the L_{PS_C} and the L_{PS} , and may use the L_{PS_C}/L_{PS} ratio as an index for a peritoneal function test. Herewith, a specific function test on the rate of transperitoneal water removal can be achieved.

In this case, the use of L_{PS_C}/L_{PS} described above and the volume of water removal as the test indexes achieves a detailed function test on the rate of transperitoneal water removal, which takes into consideration the activity power of the aquaporins.

Brief Description of the Drawings

FIG. 1 is an explanatory diagram of a Pyle-Popovich model;

FIG. 2 is an explanatory diagram of a Three-Pore Theory model;

FIG. 3 is a schematic diagram of an applied example of the present invention—a peritoneal dialysis planning apparatus using a PC;

FIG. 4 shows a flow of an embodiment using the peritoneal dialysis planning apparatus;

FIG. 5 shows an example of a time chart of a peritoneal test;

FIG. 6 shows input data items of the peritoneal test;

FIG. 7 shows input data items of the peritoneal test;

FIG. 8 is a flow diagram of a peritoneal function program of the present invention;

FIG. 9 is a graph showing a correlation between $MTAC_{un/c}$ and the volume of water removal (sample);

FIG. 10 is a graph showing a correlation between $MTAC_{un/c}$ and $L_P S_C / L_P S$ (sample);

FIG. 11 is a graph showing a correlation between $MTAC_{un/c}$ and $L_P S_C / L_P S$ (with a display of areas according to peritoneal function diagnoses) (sample);

FIG. 12 is a graph showing a correlation between $L_P S_C / L_P S$ and the volume of water removal (sample);

FIG. 13 is a flowchart of exemplified steps of a program, from data input to display of peritoneal function;

FIG. 14 is a flowchart illustrating a specific computational process of a Genetic Algorithm and the Three-Pore Theory;

FIG. 15 shows an example of a time chart of a peritoneal test; and

FIG. 16 shows a comparison between clinical data.

Detailed Description of the Invention

1. FIRST EMBODIMENT

Here is described a first embodiment of the present invention.

The peritoneal dialysis planning apparatus of the present invention (i) computes two mathematical models known as peritoneal dialysis models, (ii) processes the results of computations, and (iii) outputs and displays the processed results. Peritoneal dialysis models include a macroscopic model called the Pyle-Popovich model and a microscopic model based on the Three-Pore Theory. First, a brief description of these models is provided here.

1.1 Mathematical Models of Peritoneal Dialysis

FIG. 1 is a cross-sectional view of a peritoneum, concisely illustrating the Pyle-Popovich model. The transfer of solutes from the body fluid to the dialysis solution via the peritoneum, which is assumed to be a homogeneous membrane, is

represented by the sum of diffusion of solute molecules into the dialysis solution and convection (mass transfer due to water movement—that is, convective transport, and a back flow due to absorption of the lymphatic system in the peritoneum), as shown by arrows in the figure. This mathematical model can be expressed as the following set of formulae (1-1) to (1-8) of the mathematical expression I.

[*Mathematical Expression I*]

$$G - \frac{dV_B C_B}{dt} - C_{LR} C_B = \frac{dV_D C_D}{dt} = \dot{m} \quad (1-1)$$

$$\dot{m} = KA(C_B - C_D) + Q_U(1 - \sigma)\bar{C} \quad (1-2)$$

$$\bar{C} = C_B - f(C_B - C_D) \quad (1-3)$$

$$f = \frac{1}{\beta} - \frac{1}{\exp(\beta) - 1} \quad (1-4)$$

$$\beta = \frac{(1 - \sigma)Q_U}{KA} \quad (1-5)$$

$$Q_U = a_1 \exp(a_2 t) + a_3 \quad (1-6)$$

$$V_D(t) = V_D(0) + \frac{a_1}{a_2} [\exp(a_2 t) - 1] + a_3 t \quad (1-7)$$

$$V_B + V_D = V_B(0) + V_D(0) \quad (1-8)$$

where t: time [*min*];

C_{LR} : residual renal function [*mL/min*];

C_B : concentration of a solute in blood [*mg/mL*];

C_D : concentration of a solute in the dialysis solution [*mg/mL*];

V_B : volume of body fluid [*mL*];

V_D : volume of the drained fluid [*mL*];

β : Peclet number [—];

Q_U : ultrafiltration rate (volume of ultrafiltration) [*mL/min*];

G : solute production rate [*mg/min*];

KA : overall mass transfer—area coefficient of peritoneum (*MTAC*) [*mL/min*];

σ : Staverman reflection coefficient [—];

- a_1 : empirical constant determining Q_U [mL/min];
- a_2 : empirical constant determining Q_U [l/min]; and
- a_3 : empirical constant determining Q_U [mL/min].

Thus, the Pyle-Popovich model is based on a mass balance equation of individual solutes in the body fluid and those in the dialysis solution. In the Pyle-Popovich model, items calculated for each patient are: overall mass transfer—area coefficients KA of individual solutes, such as glucose, urea nitrogen, and creatinine (or alternatively, overall Mass Transfer-Area Coefficient, or $MTAC$); σ (Staverman reflection coefficients); and water removal parameters, a_1 , a_2 and a_3 . Of them, the water removal parameters a_1 , a_2 and a_3 are said to be particularly important for evaluating patient's capability of removing water (referred to as "the rate of transperitoneal water removal").

Empirical equations derived by Hume and Weyers can be used to calculate the volume of body fluid (V_B) (Hume *et al.*, 1971). According to sex, the empirical equations are expressed in terms of height [HT (cm)] and weight [WT (Kg)] of a patient as follows:

$$\text{Male: } V_B(0) = -14.249 + 0.19678HT + 0.29571WT; \text{ and}$$

$$\text{Female: } V_B(0) = -9.9260 + 0.17003HT + 0.21371WT.$$

In contrast with the Pyle-Popovich model, when peritoneal function is microscopically observed, there are considered to be partial variations in the permeability of each capillary vessel in the peritoneum. A peritoneal dialysis model on the basis of this perspective is the model of the Three-Pore Theory.

FIG. 2 is a schematic diagram of the capillary vessel, illustrating the model of the Three-Pore Theory. The Three-Pore Theory assumes that there are pores in three different sizes (large pores, small pores, and cell pores) in the capillary vessel. In this case, the pores act like a sieve because of the difference in size, and therefore the types and amounts of solutes which can pass through pores of specific sizes are regulated. For the same reason, pores of each size have a different contribution rate for water

removal. Accordingly, in the Three-Pore Theory, the water transfer rates (filtration rates) are calculated for pores of large, medium, and small sizes, respectively, and the total water flow rate (total ultrafiltration rate) is then obtained. This mathematical model can be expressed as the following set of formulae (2-1) to (2-4) of the mathematical expression II, and the mathematical expressions III, IV and V.

[*Mathematical Expression II*]

$$Q_U = J_{VC} + J_{VS} + J_{VL} - J_{V \text{ lymph}} \quad (2-1)$$

$$J_{VC} = L_P S_C \cdot (P_{\text{capill}} - \pi_{\text{prot}} - P_{\text{ip}} - \pi_{\text{gluc}} - \pi_{\text{urea}} - \pi_{\text{Na}} - \pi_{\text{anions}}) \quad (2-2)$$

$$J_{VS} = L_P S_S \cdot (P_{\text{capill}} - \sigma_S \pi_{\text{prot}} - P_{\text{ip}} - \sigma_S \pi_{\text{gluc}} - \sigma_S \pi_{\text{urea}} - \sigma_S \pi_{\text{Na}} - \sigma_S \pi_{\text{anions}}) \quad (2-3)$$

$$J_{VL} = L_P S_L \cdot (P_{\text{capill}} - P_{\text{ip}}) \quad (2-4)$$

where J_{VC} , J_{VS} , J_{VL} : ultrafiltration rates for cell pores (aquaporins), small pores, and large pores, respectively [mL/min];

$J_{V \text{ lymph}}$: lymphatic absorption flow rate [mL/min];

$L_P S_C$, $L_P S_S$, $L_P S_L$: water permeability coefficients for cell pores, small pores, and large pores, respectively;

π_{prot} , π_{gluc} , π_{urea} , π_{Na} , π_{anions} : osmotic pressures of protein, glucose, urea, sodium, and anions, respectively [$mmHg$];

P_{capill} : hydrostatic pressure [$mmHg$];

P_{ip} : hydrostatic pressure of the dialysis solution in the peritoneum [$mmHg$]; and

σ_S : reflection coefficient [—].

[*Mathematical Expression III*]

$$J_{V \text{ lymph}} = -Q_U(t_{\text{VAR}}) = -L_P S [P_{\text{ca}} - P_{\text{ip}} - \sigma_{\text{prot}}(\pi_{\text{p}} - \pi_{\text{ip}})]$$

where t_{VAR} : time of when the crystalloid osmotic pressure gradient is lost [min]; and

P_{ca} : hydrostatic pressure exerted on capillary endothelial cells [$mmHg$].

[Mathematical Expression IV]

$$V_D(t+\Delta t) = V_D(t) + \Delta t \cdot (J_{VC} + J_{VS} + J_{VL} - J_{lymph})$$

[Mathematical Expression V]

$$L_P S = L_P S_C + L_P S_S + L_P S_L \quad (5-1)$$

$$L_P S = \frac{0.070 \cdot \frac{A0}{\Delta x}}{23000} \quad (5-2)$$

where $L_P S$: water transport rate of the peritoneum (ultrafiltration coefficient) [$mL/min/mmHg/1.73 m^2$]; and
 $A0/\Delta x$: area parameter [$cm/1.73 m^2$].

Note that $A0/\Delta x$ and $L_P S_C$ in the formulae (5-1) and (5-2) of the mathematical expression V are unknown parameters unique to each patient. Some methods for approximating these parameter values in the Three-Pore Theory model have been proposed, including the modified Powell method. Here, data is collected from dialysis solutions with two or more different osmotic pressures and the above-mentioned parameters are calculated using the modified Powell method. However, a different method may be employed for the calculation. Although the Pyle-Popovich model is capable of carrying out analysis by using two sets of data, the Three-Pore Theory model requires many more sets of data to find the parameters of $A0/\Delta x$ and $L_P S_C$ by repetitive calculations using the modified Powell method.

Note that cell pores are considered as aquaporins (H_2O channels), and are essential since they make a contribution accounting for as much as 40% of the entire volume of water removal. The aquaporins have a very important correlation with the rate of transperitoneal water removal of a patient since they are irreversible and cannot be returned to the original state once being broken. Therefore, in dialysis treatments, how to retain the aquaporins without rendering them ineffective is a key issue to maintain peritoneal function.

Each of $L_P S$ items ($L_P S_C$, $L_P S_S$ and $L_P S_L$) is a water permeability coefficient, while $L_P S$ is called an overall water permeability coefficient. These coefficients

taking large values indicates that the rate of transperitoneal water removal is high. Especially, a high value in $L_P S_C$ is considered that the rate of transperitoneal water removal of the patient has been maintained relatively well. Accordingly, it is very important to examine closely values of the water permeability coefficients when peritoneal function of patients is studied by using the Three-Pore Theory.

In the Three-Pore Theory, a current osmotic pressure can be obtained by updating the concentration gradient of each solute at the present moment, and also the water transfer rate is newly calculated. Then, further calculation together with the value of total peritoneal area is performed with respect to each patient, which enables construction of a detailed model of the solute transfer and the volume of water removal.

1.2 Configuration of Peritoneal Dialysis Planning Apparatus

Next is described the configuration of the peritoneal dialysis planning apparatus of the first embodiment according to the present invention. The peritoneal dialysis planning apparatus can be formed by implementing a program for executing a peritoneal dialysis testing method (a program for testing peritoneal function) on a general-purpose computer.

FIG.3 shows a structural example of the peritoneal dialysis planning apparatus of the present invention. Here is shown a personal computer (PC) 1 comprising: a main body 11 having publicly known CPU, HD and memory therein; a keyboard 12 connected to the main body as input means; and a display 10 serving as data output means (display unit). The peritoneal function testing program of the present invention may be, for example, read to the PC 1 from various transportable recording media 20 (a CD-ROM 201, a DVD-ROM 202, a flexible disc 203, and a memory card 204), or may be read to the PC 1 from a storage device 30, such as a different server or PC, via a communication line. It is desirable that the peritoneal function testing program, once being read, be stored in the HD of the PC 1, along with patient's data.

The peritoneal dialysis planning apparatus uses a range of data obtained from

a patient in a general test (for example, Peritoneal Equilibration Test, or PET) as input data. The CPU of the PC 1 computes mathematical models of peritoneal function (the Pyle-Popovich model, or both the Pyle-Popovich model and the Three-Pore Theory model), and performs processing specific to the first embodiment on data pertaining to the concentration of each solute, the volume of water removal and the like which are obtained as a result of the computation. Then, the CPU presents the processed data on the display 10. The presented contents on the display 10 assist consideration of the future peritoneal dialysis planning. Herewith, the peritoneal dialysis planning apparatus of the present invention is characterized in that the state of peritoneal function over time (a mechanism of deterioration in peritoneal function) can be tested in an appropriate manner.

Note that the peritoneal dialysis planning apparatus has an advantage of making an effective use of conventional devices and data from the past, not requiring other special devices, calculation methods, new data which has previously never been used or the like, to perform the function.

1.3 Configuration of Peritoneal Function Testing Program

The peritoneal function testing program implemented on the PC 1 is configured to be generally executed in the following sequence. FIG. 4 shows a sequence of the program, from input of the data to display of the peritoneal function.

As shown in the figure, first, patient's clinical data required for the peritoneal function test is input to the PC 1. The program becomes executable after the data is input, and computes the Pyle-Popovich model according to an operator's direction. The *MTAC* ratio ($MTAC_{un/c}$) of urea nitrogen and creatinine is obtained by using parameters acquired from the computation, such as solute concentrations and the volume of water removal, and a graph showing a correlation between $MTAC_{un/c}$ and the volume of water removal is presented on the display 10. This enables the operator to conduct a study on peritoneal function. The main feature of the present invention is to use $MTAC_{un/c}$ and $L_P S_C / L_P S$ —which is described hereinafter—as indexes of the

peritoneal function test. Effectiveness of $MTAC_{un/c}$ and details about $MTAC_{un/c}$ and $L_P S_C/L_P S$ are described in more depth when the operational sequence is discussed.

The program can complete the work once when the graph of the correlation between $MTAC_{un/c}$ and the volume of water removal is presented on the display 10. However, the program performs further computation to make a more precise investigation for the peritoneal function test at operator's request. In this case, the PC 1 checks if the amount of the obtained data sets is sufficient (specifically speaking, three or more data sets in relation to dialysis solutions with multiple osmotic pressures are required), and then computes the Three-Pore Theory model. By using water permeability coefficients and other parameters obtained from the computation, a correlation between $MTAC_{un/c}$ and $L_P S_C/L_P S$ together with the volume of water removal computed earlier as well as a correlation between $L_P S_C/L_P S$ and the volume of water removal are displayed in graphs. This enables the operator to conduct a detailed study on peritoneal function.

Regarding the patient's data to be input, it is desirable that all items required to calculate both the Pyle-Popovich model and the Three-Pore Theory model be prepared in sufficient quantities and set ready to be input to the PC 1 prior to the program being run, which allows prompt computations.

1.4 Practical Example

In order to make the apparatus work, data obtained from a patient is required. A method for acquiring the data is first described prior to a description of the apparatus operations.

1.4.1 Acquisition and Input of Clinical Data

Here are shown a procedure for the above-mentioned peritoneal function test (clinical test) of the present invention and an example of data acquisition steps. FIG. 5 shows the steps for the data acquisition. In the data acquisition steps, dialysis solution exchange, which starts in the evening of a previous day, is performed on a patient six times in total at intervals of 10.5 hours, 4 hours, 3 hours, 5 hours and 2

hours, by alternately using dialysis solutions both having 2 liters in volume but one with an osmotic pressure of 360 (mOsm/kg-solvent) while the other having an osmotic pressure of 400 (mOsm/kg-solvent). Here, a blood sample is taken on a regular schedule, and a urine sample is collected while the concentration of each solute is checked. The osmotic pressures of the dialysis solutions and the number of exchanges can take values other than the above. Note that the example shown here uses dialysis solutions having two different osmotic pressures, which is necessary for computing the formulae of both the Pyle-Popovich and the Three-Pore Theory. Here, the computation of the Pyle-Popovich formulae requires at least two different sets of data on drained fluids with each osmotic pressure, while the computation of the Three-Pore Theory formulae requires at least three different sets of data for drained fluids with each osmotic pressure, and therefore appropriate settings should be configured to comply the data acquisition.

The items of clinical data obtained through the data acquisition steps include the height, weight and sex of the patient, the amount of collected urine, and the concentration of each solute in urine (urinary urea nitrogen, urinary creatinine, urinary protein, and urinary sodium), as shown in FIGs. 6 and 7. The exact same tables of the figures are presented on the display 10 of the peritoneal dialysis planning apparatus 1, and each item can be input via the input means (i.e. keyboard) 12. The operator of the PC 1 enters the input items of FIGs. 6 and 7.

The input items include the concentrations of blood-total protein, albumin, serum creatinine, urea nitrogen, glucose, sodium, chloride and so on, obtained from the blood samples. In this case, blood sampling is performed three times and therefore concentration measurements are repeated with respect to each input item when a blood sample is collected, and then the values are entered.

Note that, in the present embodiment, the presentation of a graph becomes possible by using numerical values obtained from at least three data sets on the drained fluids.

In terms of the drained fluids, the glucose concentration, the total weight of medical solution, the drainage start time, the patient's weight after the drainage, the finish time of injecting a dialysis solution and so on are recorded.

1.4.2 Operation of Peritoneal Dialysis Planning Apparatus

Once the input of the above individual pieces of data to the peritoneal dialysis planning apparatus is completed, the program of the peritoneal dialysis planning apparatus (a peritoneal function testing program) can be executed.

FIG. 8 is a flow diagram showing exemplified steps of the peritoneal function testing program.

According to the figure, the program is first launched on the PC 1, which then judges whether or not data required to compute the Pyle-Popovich model has been input (Step S101).

If the input data has sufficiently been provided, the PC 1 computes the Pyle-Popovich model shown in the above mathematical expression I, based on the input patient's data (Step S102). This computation determines the overall mass transfer—area coefficients for urea nitrogen ($MTAC_{un}$) as well as for creatinine ($MTAC_c$), the volume of water removal and so on. Note that how to compute the simultaneous equations of the Pyle-Popovich model is described in Japanese Laid-Open Patent Application Publication No. 2000-140100. Here, the PC 1 characteristically calculates the ratio ($MTAC_{un/c}$) of $MTAC_{un}$ to $MTAC_c$ obtained from the computation of the Pyle-Popovich model, and presents a graph showing the correlation between the $MTAC_{un/c}$ ratio and the volume of water removal on the display 10 (FIG. 9) (Step S103).

Focusing on the transfer rate of each solute ($MTAC$) derived from the Pyle-Popovich model, the present inventors have for the first time discovered the $MTAC_{un/c}$ ratio that is a mass transfer parameter effectively applicable as a dramatically more precise peritoneal function testing and therapeutic indication of individual patients.

In other words, $MTAC_{un}$ and $MTAC_c$ respectively are quantitative indexes of publicly known overall mass transfer—area coefficients, and each value indicates, only on a piecemeal basis, the peritoneal function of a patient of when data was obtained. Doctors cannot comprehend details of the state of patient's peritoneal function based on these numerical values alone. In addition, as indexes for evaluating the dialysis efficiency (i.e. quantitatively evaluating the clear space), clearance, Kt/V and the like are generally used in order to determine the excess or deficiency of the amount of a dialysis solution. However, the concepts of these indexes are dissimilar, and therefore it is difficult to study peritoneal function in a comprehensive manner.

However, $MTAC_{un/c}$ indicates that, when the value is closer to 1 (i.e. the values of $MTAC_{un}$ and $MTAC_c$ are closer to each other), the patient has a higher possibility of having complications with peritonitis or having such complications in the future, or the patient has a peritoneum with deteriorated function. In all of these cases, the introduction of hemodialysis is considered as a countermeasure. The validity of such judgment can be proved by empirical data obtained from patients actually having complications with peritonitis and patients likely to have the complications in the future (data showing that patients having complications with peritonitis have a deteriorated level of permeability of the peritoneum is provided in a paper (*Advances in Peritoneal Dialysis*, vol. 18, pp. 144-148, 2002)). That is, although conventional testing is capable of analyzing only quantitative indexes, the present invention is able to perform time-lapse diagnoses of the peritoneum. Additionally, since $MTAC_{un/c}$ is a dimensionless ratio, the parameter need not be adjusted for variations in physical attributes of individual patients, and furthermore offers a high versatility since it can be used in the Pyle-Popovich model as well as formulae based on other concepts. Note that $L_P S_C / L_P S$, as will hereinafter be described, is also a dimensionless parameter, and offers an expanded versatility.

Besides, the first embodiment is capable of performing more detailed testing on peritoneal function by making a graph plotting $MTAC_{un/c}$ against the volume of

water removal, as shown in FIG. 9. Here, a dialysis solution with a glucose concentration of 2.5% is used, and the volume of water removal is plotted on the vertical axis while $MTAC_{un/c}$ is plotted on the horizontal axis. According to the graph, values of $MTAC_{un/c}$ and the volume of water removal of when the data was obtained can be checked virtually simultaneously. Therefore, for example in the case when the volume of water removal is low, even if $MTAC_{un/c}$ is favorable, a reduction in peritoneal function other than the solute transfer (i.e. mainly, the rate of transperitoneal water removal) can be determined. This leads to an examination of the adequacy of switching to an efficient dialysis procedure in which unnecessary use of antiphlogistic drugs for peritonitis is avoided (i.e. a switch to hemodialysis from peritoneal dialysis). When neither $MTAC_{un/c}$ nor the volume of water removal is favorable, it is determined that peritoneal function has been severely damaged causing malignant failure, which allows a prompt transition of the dialysis procedure and quick countermeasures along with prescription of various antiphlogistic drugs. In the case when the volume of water removal is favorable, while $MTAC_{un/c}$ is low, it is determined that peritoneal function is in a benign failure mode (that is, although the aquaporins are sufficiently active, the small and large pores with reversibility are exhausted and temporarily deactivated), which raises consideration of the necessity of rest.

Note that FIGs. 9 to 12 plot actual measurements obtained from multiple patients and show the distributions. A line in each graph represents a regression line of the graph. Values of y , r and p in each graph are numerical values indicating characteristics of the measurement distribution. Such lines provide indications of peritoneal function of a patient. (For example, assume that the volume of water removal of a patient is located below the line. This means that the patient has a lower rate of transperitoneal water removal than the average.) In addition, such lines may offer an advantageous effect when data of multiple patients or multiple pieces of time-lapse data of a single patient are displayed.

Thus, the first embodiment is able to obtain information on the mechanism of

deterioration in peritoneal function of a patient from various angles by making a graph of a correlation between $MTAC_{un/c}$ and the volume of water removal, which allows appropriate evaluations. The data of FIG. 9 can be derived only from the Pyle-Popovich model, and thus there is an advantage of obtaining the data by comparatively simple testing and computations. In addition, since $MTAC_{un/c}$ is acquired from $MTAC_{un}$ and $MTAC_c$ —existing data which has conventionally been collected, the present invention makes an effective use of the past data without wasting them, and utilizes them as more specific and adequate testing parameters.

Note that a graph to be displayed in Step S103 is here set to the graph of $MTAC_{un/c}$ v.s. the volume of water removal. However, it is also possible to display data of $MTAC_{un/c}$ alone by selection from the display setting items of the program.

In the comparatively simple peritoneal function testing, the graph of FIG. 9 showing a correlation between $MTAC_{un/c}$ and the volume of water removal allows some degree of examination, as described above. Consequently, the PC 1 prompts the operator to decide whether or not to complete the testing (Step S104). At this point, if the operator desires to have more detailed peritoneal function testing, the PC 1 executes the program to proceed to the next step.

In the following step, the PC 1 checks if a sufficient amount of data is present (Step S105). This step is taken in order to see if the amount of data is enough to solve Three-Pore Theory model. When there is enough data (that is, if data on dialysis solutions of two or more osmotic pressures has been input), the PC 1 computes the Three-Pore theory model shown in the above mathematical expressions II to V, based on the input patient's data (Step S106). Here, the PC 1 characteristically calculates the ratio ($L_P S_C / L_P S$) of the water permeability coefficient of aquaporins to the overall water permeability coefficient, and makes a graph of a correlation between, e.g., $L_P S_C / L_P S$ and previously calculated $MTAC_{un/c}$, which is then presented on the display 10 (FIG. 10) (Step S107).

Note that, although the graph of $MTAC_{un/c}$ v.s. $L_P S_C / L_P S$ (FIG. 10) is presented

here in the process flow, a graph desired by the user—i.e. any one of $MTAC_{un/c}$ v.s. $L_P S_C / L_P S$ (FIG. 10), $MTAC_{un/c}$ v.s. $L_P S_C / L_P S$ with peritoneal function states labeled (FIG. 11), and $L_P S_C / L_P S$ v.s. the volume of water removal (FIG. 12)—can be presented on the display 10 by modifying the display setting of the program.

Thus, the first embodiment is capable of performing further detailed peritoneal function testing by calculating the ratio ($L_P S_C / L_P S$) of the dynamic water permeability coefficient of aquaporins to the overall water permeability coefficient obtained from the computations of the Three-Pore Theory. The $L_P S_C / L_P S$ ratio represents the activity power of the aquaporins, which is believed to account for approximately 40% of the rate of transperitoneal water removal in pores in the capillary vessels of the peritoneum. The ratio taking a larger value means that the rate of the transperitoneal water removal is higher. A detailed diagnosis of peritoneal function is made possible by presenting a correlation of $L_P S_C / L_P S$ with $MTAC_{un/c}$ or with the volume of water removal.

Namely, for example, when the value of $L_P S_C / L_P S$ is not favorable, the reason is thought to be attributable to a decrease in activity of the aquaporins. In general tests of the rate of transperitoneal water removal, on the other hand, a patient is examined mainly based on data of an apparent volume of water removal obtained in CAPD. In this case, if the volume of water removal is low, multiple possible causes as follows can be in fact deduced, making it difficult to determine which of the following causes is/are the actual cause:

A: water is not drained out since the catheter tip inserted into the peritoneum is physically blocked or malpositioned (external factor);

B: the lymphatic system of the peritoneum has an elevated level of reabsorption capability; and

C: actual peritoneal function (the rate of transperitoneal water removal) has been reduced.

Of them, when *A* is the real cause, the blockage in the catheter is removed or

the position is corrected, while anti-inflammatory agents are administered into the lymphatic system when B is the cause. If the cause is C , dialysis modality is switched from peritoneal dialysis to hemodialysis. Thus, the ways of handling the situation are much different depending on the real cause. In addition, when both B and C are the causes, the patient may possibly have complications with peritonitis or encapsulated peritoneal sclerosis, and therefore much consideration has to be given to how to treat the patient.

Thus, conventional methods of testing peritoneal function do not fully allow critical judgments to be made to determine appropriate treatments for patients, and therefore, there is still room for improvement. On the other hand, the present invention using $L_P S_C / L_P S$ that is a parameter independent of the above causes A and B is capable of comprehending the rate of transperitoneal water removal of a patient with dramatically improved accuracy. Here, $L_P S_C / L_P S$ of the present invention is calculated based on data collected from a patient, and determined as a dynamic ratio unique to an individual patient. With regard to $L_P S_C / L_P S$, there are conventional systems in which peritoneal function testing is carried out by using the ratio (for example, a peritoneal function testing system manufactured by Gambro). However, the ratio is specified as a fixed value (1) and does not reflect specific peritoneal function of each patient. A method of using the dynamic $L_P S_C / L_P S$ ratio as a testing index was constructed, for the first time, in the present invention.

Here, FIG. 10 presented on the display 10 in Step S107 is a graph plotting $MTAC_{un/c}$ against $L_P S_C / L_P S$, which are acquired by computing the Pyle-Popovich model and the Three-Pore Theory model. In FIG. 10, $L_P S_C / L_P S$ indicates a more accurate rate of transperitoneal water removal than an apparent volume of water removal obtained by CAPD. It can therefore be said that the graph shows data with a higher level of accuracy than the data of FIG. 9, which is derived only from the Pyle-Popovich model described above. The present invention also has an advantageous effect of allowing a choice between computing only the Pyle-Popovich model or computing the

model in combination with the Three-Pore Theory model, depending on whether a higher priority is placed on simplicity or accuracy when peritoneal function of a patient is examined.

Note that it is effective to roughly divide the area of a graph into sub-areas according to states of peritoneal function when the graph is displayed since this provides a rough indication for the location of obtained data in the graph. FIG. 11 shows an example in which the area of the coordinates of the graph in FIG. 10 above is divided into sub-areas of "good water removal", "benign failure/rest of the peritoneum required", "a follow-up required" and "malignant failure", according to the states of peritoneal function. Here, the boundary on the horizontal axis between "good water removal" and "benign failure/rest of the peritoneum required" and the boundary on the vertical axis between "malignant failure" and "benign failure/rest of the peritoneum required" are determined individually by likely values that $MTAC_{un/c}$ and $L_P S_C/L_P S$ would take when the volume of water removal is approximately 500 mL (in general, when the volume of water removal reaches 500 mL, switching from a peritoneal dialysis to hemodialysis is recommended). The present invention may, thus using such categories, allow a rough assessment of the state of peritoneal function to be made according to the location of the collected data in the category map. It is a matter of course that the position of each boundary, the type of line used to represent the data in a category map, words used to label the categories can be changed accordingly.

$L_P S_C/L_P S$ basically has a property of being proportional to the rate of transperitoneal water removal. Therefore, if a graph is created with these parameters plotted on the horizontal and vertical axes, respectively, the possibility that water removal is not properly being performed can be assessed when there is no proportional relationship between $L_P S_C/L_P S$ and the volume of water removal of the obtained data. FIG. 12 is a graph showing a correlation between $L_P S_C/L_P S$ and the volume of water removal in such a case. According to a graph like this, for example, when $L_P S_C/L_P S$ is

favorable while the volume of water removal is low, the following possibilities can be considered: the lymphatic system has an elevated level of reabsorption capability; and water cannot be removed since the catheter is blocked, malpositioned, or contaminated. Accordingly, it is made possible to prescribe a medicine to reduce the elevated level of the reabsorption by the lymphatic system when the former is the cause, or to advise the patient on an appropriate CAPD procedure and instrument management when the latter is the cause. The PC 1 here completes the entire process flow.

Note that, in the steps for displaying data (Steps S103 and S107) described above, it can also be made possible to provide selection of whether or not the above-described boundaries roughly indicating states of peritoneal function and words used to label the categories are displayed on the graph together with the patient's data.

Once displaying a graph desired by the operator in Step S107, the PC 1 can terminate the program.

2. SECOND EMBODIMENT

2.1 *Main Characteristics of Second Embodiment*

A second embodiment of the present invention is described next.

The configuration of a peritoneal dialysis planning apparatus and basic operations of a peritoneal function testing program (including items on the screen display) according to the second embodiment are the same as those in the first embodiment, and therefore the following discusses the second embodiment, focusing on differences from the first embodiment.

The second embodiment is characterized by achieving a peritoneal function test of higher precision by applying, in the peritoneal function testing program installed on the PC 1, a Genetic Algorithm (GA) to parameter values obtained from the computation of the Pyle-Popovich model to thereby make them an optimal solution for actual measurements of clinical data in advance, and then introducing the solution to the formulae of the Three-Pore Theory.

In addition, by adopting the Genetic Algorithm, the computation of the Pyle-Popovich model becomes simplified and a reduction in the quantity of clinical data required is achieved. This in turn brings about an effect of easing the burden of patients and data examiners of when clinical data is collected.

Note that the Genetic Algorithm itself is a well-known mathematical model used as a search technique to find an optimal solution. The details are discussed in, for example: "*Iden Algorithm to Saiteki-ka* (Genetic Algorithm and Optimization)" (edited by the Institute of Systems, Control and Information Engineers, and published by Asakura-syoten on 15 April 1998); "*Iden-teki Programming Nyumon* (Introduction to Genetic Programming)" (by Hitoshi IBA, published by University of Tokyo Press in July 2001); and "*Iden Algorithm to Neural Network—Scheduling to Kumiawase Saiteki-ka* (Genetic Algorithm and Neural Network—Scheduling and Combined Optimization)" (edited by Denki-gakkai Iden Algorithm nado Kumiawase Saiteki-ka Syuho Ohyo Chosa Senmon Iinkai (Expert Committee on Investigation of Genetic Algorithm and Other Combined Optimization Method Application at the Institute of Electrical Engineers of Japan), published by Corona-sha in January 1998).

Specifically speaking, the second embodiment deals with overall mass transfer—area coefficients KA of individual solutes—such as, glucose, urea nitrogen and creatinine—obtained from the computation of the Pyle-Popovich model. In other words, $MTAC_{glc}$ ($MTAC$ of glucose), $MTAC_{urea}$ ($MTAC_{un}$), and $MTAC_{crea}$ ($MTAC_c$), and furthermore a water permeability coefficient ratio $rL_P S_C$ are treated as discrete parameters varying independently of one another. The ratio $rL_P S_C$ is, as shown in the mathematical expression VI below, directly obtained by transforming the formula (5-1) of the above mathematical expression V.

[*Mathematical Expression VI*]

$$rL_P S_C = \frac{L_P S_C}{L_P S}$$

$MTAC_{glc}$, $MTAC_{un}$ and $MTAC_c$ for each solute and $rL_P S_C$, in reality, tend to vary

largely according to peritoneal function of individual patients, and they individually take values specific to each patient. Taking this point into account, the second embodiment explicitly treats these four parameters as dynamic variables, and enables more precise and accurate dialysis planning to be performed according to peritoneal function of individual patients.

Note that multi-dimensional equations need to be solved here since the above new parameter is added, which leads to an increase in the computational freedom. As a result, the peritoneal function testing program of the first embodiment with no modification cannot cover the increased freedom of computation. To reduce the computational burden, in the peritoneal function testing program of the second embodiment, computation of the Three-Pore Theory formulae in combination with the Genetic Algorithm is carried out on the results obtained by calculating the Pyle-Popovich model, which facilitates to narrow the parameter values to the optimal solution. Since the Genetic Algorithm is a technique for converging the computation outcome to the optimal solution, with the use of evaluation functions, by repeating a specific amount of computation for provided initial estimate values, the use of the Genetic Algorithm enables rather quick computation.

2.2 Configuration and Operations of Peritoneal Function Testing Program

The peritoneal function testing program of the second embodiment is configured to be generally executed in the following sequence. Here is described the program configuration together with a practical example including how to collect clinical data.

FIG. 13 is a flow diagram showing exemplified steps of the peritoneal function testing program, from data input to display of peritoneal function. "PPM" in the figure means the Pyle-Popovich model while "TPT" denotes the Three-Pore Theory. A main characteristic of this process flow is a GA-TPT computation step (Step S3).

According to the process flow shown in FIG. 13, when the program is executed, the operator inputs patient's clinical data required for the peritoneal function test to the

PC 1 of the peritoneal dialysis planning apparatus. The data items are as shown in charts of FIGs. 6 and 7. However, in the second embodiment, only the amount of total protein may be measured while the measurement of albumin in drained fluid being omitted. This is because the concentration of albumin in drained fluid is proportional to the concentration of total protein. Alternatively, it is possible to obtain the amount of albumin from the amount of total protein.

A schedule (time chart) for collecting necessary clinical data is characterized by starting, for example, at 1 o'clock in the afternoon on the previous day of a hospital visit, with acquisition of data on the amount of drained fluid and the amount of collected urine performed by a patient himself, and finished with one-time-only blood sample collection carried out when the patient visits the hospital on the next day (1:00 p.m.), as shown in FIG. 15.

In the second embodiment, the required clinical data is reduced to the amount that can be collected in one hospital visit of a patient—to be specific, the number of clinical data sets is reduced to four (i.e. the number of dialysis solution exchanges) and the blood sampling is limited to once, as shown in a comparative diagram of FIG. 16. The clinical data collection at hospital can be carried out together with a regular medical checkup, and thus the second embodiment can reduce not only patient's burden and labor but also the workload of staff collecting clinical data, as compared to the first embodiment. This is because only a smaller number of data sets are required for computation thanks to the adoption of the Genetic Algorithm to the program, which is described hereinafter.

When the input of the above data is complete, the peritoneal function testing program becomes executable. Then, if the amount of the input data is sufficient in just proportion (Step S1), the program carries out a first computational step—computation of the Pyle-Popovich model—according to the operator's direction (Step S2).

Here, the computation of the Pyle-Popovich model is basically executed in the

same process as in the first embodiment. However, in the second embodiment, the formula (1-2) of the mathematical expression I is simplified.

Namely, it is here assumed that the blood concentration of solutes during the dialysis is fairly constant, and therefore an approximate constant is assigned to C_B in the formula (1-2). Herewith, only C_D is virtually a variable in the formula (1-2), which simplifies the formula to be a linear differential equation. Such simplification of making the formula (1-2) be a linear differential equation is justified based on the judgment that assigning an approximate value to C_B at this point has no significant effect on the final result in the case where the computed results of the Pyle-Popovich model are treated as initial estimate values for the calculation of the Three-Pore Theory formulae.

Note that simplifying the formula (1-2) to a linear differential equation is not indispensable for the present invention. However, without the simplification, the same number of clinical data sets is required as in the first embodiment.

From the results of the Pyle-Popovich model obtained in this way, the respective parameter values including $MTAC_{glc}$, $MTAC_{un}$, $MTAC_c$, σ , a_1 , a_2 , a_3 and $rLPS_C$ are, as in the first embodiment, calculated. Of them, the values of $MTAC_{glc}$, $MTAC_{un}$, $MTAC_c$ and $rLPS_C$ are used as an unknown parameter set (initial estimate values) for the computation of the Three-Pore Theory.

After obtaining values of the individual parameters above, computation of the Genetic Algorithm and the Three-Pore Theory (GA-TPT computation) is carried out as a second computational step, which is a characteristic of the present embodiment (Step S3). Here, an elite parameter set (an optimal solution) is obtained from the unknown parameter set (initial estimate values) through the computation of the Genetic Algorithm, and then the formulae of the Three-Pore Theory are solved using the elite parameter set.

FIG. 14 is a flowchart specifically illustrating a process of the computation of the Genetic Algorithm and the Three-Pore Theory (GA-TPT computation) in Step S3.

As shown in the figure, in Step S3, the PC 1 prepares multiple parameter sets through coding operations using the Genetic Algorithm, based on the parameter set (the initial estimate parameter set) which comprises four unknown parameters obtained from the Pyle-Popovich model above (Step S301). Here, the initial estimate parameter set itself may be included in the prepared multiple parameter sets.

Next, the PC 1 computes the Three-Pore Theory by using each of the multiple parameter sets (Step S302). The computation of the Three-Pore Theory is carried out in the same manner as in the first embodiment, using the mathematical expressions II to V. Then, the PC 1 performs error evaluation for the computational result of each parameter set. For the error evaluation, an error calculation method is employed in which the following formulae (7-1) and (7-2) of the mathematical expression VII are used as evaluation functions, and an estimated amount of drained fluid V_{DEST} and an estimated concentration of solution in the drained fluid C_{DsEST} are respectively checked against actual measurements (V_{DCLN} , C_{DsCLN}).

[*Mathematical Expression VII*]

$$Err_{VD} = \Sigma \frac{(V_{DEST} - V_{DCLN})^2}{V_D(0)} \quad (7-1)$$

$$Err_{CDs} = \Sigma \frac{(C_{DsEST} - C_{DsCLN})^2}{C_{Ds}(0)} \quad (7-2)$$

Subsequently, the PC 1 selects and leaves a parameter set with the smallest error obtained in the error evaluation of Step S302 (Step S303). The parameter set selected here is called, for example, a "quasi-elite parameter set".

Then, the PC 1 judges whether or not the error of the quasi-elite parameter set is less than a reference value (Step S304).

As one example of the reference value for the judgment in Step S304, the second embodiment requires the error of the mathematical expression VII to be less than 5%. If the error between V_{DEST} and C_{DsEST} of the quasi-elite parameter set and the actual measurements V_{DCLN} and C_{DsCLN} is as large as to be greater than or equal to the reference value—namely, 5% or more, a value of each parameter in the current

quasi-elite parameter set is crossed based on the Genetic Algorithm to create genetic offspring, while coding operations being performed to thereby prepare newly created multiple parameter sets (Step S305).

The operation procedure of the crossing includes, for example, changing each parameter value of the quasi-elite parameter set from a decimal number to a binary-coded form and making high-order and lower-order bits in each value shuffled. Note that the present invention may use a shuffling technique other than this—for example, empirically narrowing down the range of a value by using the normal distribution which indicates the existing probability of the parameter. Or alternatively, the parameter value and the error may be respectively plotted on each of crossed axes so as to create a landscape (map), and the range of the value can be narrowed down, around local minimum points shown on the map.

Then, steps of S302, S303, S304 and S05 are repeated in the stated order until the computed values of the Three-Pore Theory and the actual measurements have better fitness with the error between them reaching less than 5% in Step S304.

If the error is judged to be less than 5% in Step S304, the quasi-elite parameter set at this point is determined as an elite parameter set (an optimal solution) (Step S306), and then the process flow of the GA-PTP computation is brought to completion.

As shown in Step S4 of FIG. 13, the PC 1 subsequently outputs, to the display 10, either one of correlation diagrams pertaining to $MTAC_{un/c}$ v.s. the volume of water removal or $MTA_{Cun/c}$ v.s. $L_P S_C / L_P S$ (the same as FIGs. 9 to 12), which are created based on the results obtained from the Three-Pore Theory computation using the elite parameter set and the earlier computed results from the Pyle-Popovich model.

Thus, in the second embodiment, the initial estimate parameter set obtained from the Pyle-Popovich model is fitted according to an individual patient, then the computation of the Three-Pore Theory is carried out based on the fitted initial estimate parameter set, and the computed results are presented on a display. Therefore, the second embodiment is capable of performing accurate and detailed dialysis planning

which is further more specific to individual patients. In addition, work required of patients and data examiners to implement the second embodiment can be reduced, which in turn leads to alleviating their mental burden and letting them take a relaxed attitude toward the testing. As a result, dialysis planning may be reviewed once and again, and it is also expected to bring an effect that the best-suited dialysis plan is offered to patients each time.

It is a matter of course that the error reference in Step S304 of the above process flow can take a value other than 5%. As a rough guide for setting the reference value, it is desirable to refer to data on daily prescription (data on drained fluid, etc.) tailored to individual patients.

In addition, multiple quasi-elite parameter sets may be selected in Step S303. In this case, only one elite parameter set will be selected from the multiple quasi-elite parameter sets. When the error reaches or exceeds the reference value, crossing is performed within the multiple quasi-elite parameter sets to calculate the genetic offspring.

3. ADDITIONAL PARTICULARS

The present invention provides an example of deriving $L_P S_C / L_P S$ by using data obtained from the Three-Pore Theory model and using this ratio as an index of the peritoneal function test. Instead of the water permeability coefficient of aquaporins $L_P S_C$, however, the water permeability coefficients of pores transferring medium- and small-sized molecules $L_P S_L$ and $L_P S_S$ may be used to calculate a ratio to $L_P S$ since similar proportional relations can theoretically be observed. Practically speaking, however, pores transferring medium- and small-sized molecules have variations in the rate of transferring solutes, and problems of reproducibility are not negligible. Therefore, the use of these water permeability coefficients $L_P S_L$ and $L_P S_S$ is less recommended.

Although the first embodiment shows an example of computing the Pyle-Popovich model and the Three-Pore Theory model by using data obtained from a

patient and calculating $MTAC_{un/c}$ and $L_P S_C / L_P S$, the present invention is not limited to this. Each value of $MTAC_{un}$, $MTAC_c$, $L_P S_C$, $L_P S$ and the like already obtained by a computing unit of a different apparatus may be used as input data, and $MTAC_{un/c}$ and $L_P S_C / L_P S$ may be calculated from the input data, for example.

In addition, $MTAC_{un}$ and $MTAC_c$ can be derived from a mathematical model other than the Pyle-Popovich model.

Furthermore, in the above embodiments, the display 10 is used as an example of data output means. However, the present invention is not confined to this, and data may be output by audio using speakers.

The present invention is applicable to the study of peritoneal dialysis planning in dialysis treatment.